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1. A method of producing a selected polypeptide expressed by a host cell culture, said method comprising the steps of:

- a. expressing a fused polypeptide by culturing said host cell culture, the cells of said culture containing and being capable of expressing a recombinant DNA encoding said fused polypeptide, said fused polypeptide comprising:
- a first sequence of amino acids defining a leader sequence, a hinge region, and at least one amino acid defining a cleavage site recognizable and cleavable by a selected cleavage agent, said hinge region being cysteine-free and comprising at least two amino acids which promote cleavage by said cleavage agent at said cleavage site; and
 - a second sequence of amino acids linked to said first sequence defining a selected target polypeptide;
- b. exposing said fused polypeptide to said selected cleavage agent in an environment wherein said target

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polypeptide is disposed in its tertiary conformation and said selected cleavage agent is rendered preferentially accessible to said cleavage site by said hinge region, thereby to cleave said target polypeptide from the remainder of said fused polypeptide preferentially at said cleavage site; and

c. separating said target polypeptide from the remainder of said fused polypeptide.

2. The method of claim 1 wherein said first sequence of amino acids imparts a preselected property to said fused polypeptide operable to facilitate concentration of said fused polypeptide, and wherein prior to step b, said fused polypeptide is concentrated by exploitation of said selected property.

3. The method of claim 2 wherein said sequence of amino acids which imparts a preselected property comprises an amphiphilic helix, said method comprising the additional step of permitting said fused polypeptide to form intracellular inclusion bodies and collecting said inclusion bodies prior to step b.

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4. The method of claim 1 wherein
said cleavage site is immediately
adjacent said target polypeptide.
 5. The method of claim 1 wherein
said cleavage site comprises one or a
sequence of amino acids absent from
said target polypeptide.
 6. The method of claim 1 wherein
said cleavage site comprises a unique
one or sequence of amino acids in said
fused polypeptide.
 7. The method of claim 1 wherein
said hinge region comprises at least
one proline residue.
 8. The method of claim 1 wherein
said hinge region comprises an amino
acid sequence which forms a random coil
when said fused polypeptides is
disposed in aqueous solution.
 9. The method of claim 1 wherein
said hinge region includes a member
selected from the group consisting of
aspartic acid, glutamic acid, lysine,
arginine, serine, proline, and
combinations thereof, in amounts
sufficient to render said hinge region
soluble in water.

10. The method of claim 1 wherein said cleavage site is a glutamic acid residue and said cleavage agent is S. aureus V-8 protease.
11. The method of claim 1 wherein said second sequence of amino acids comprises an amino acid or an amino acid sequence cleavable by said cleavage agent at a rate less than the rate at which said cleavage site is cleaved, said method comprising the additional steps of:
stopping the cleavage reactions of step b prior to its completion; separating cleaved target polypeptide from the remainder of the reaction mixture; and repeating step b with the remainder of said reaction mixture.
12. The method of claim 1 wherein said cleavage agent and said cleavage site are selected from the group consisting of the cleavage agents and cleavage site pairings set forth in Table 1.
13. The method of claim 1 wherein said target polypeptide comprises at least two cysteine residues, said method comprising the additional step of subjecting said fused polypeptide prior to step b to oxidizing conditions so that said selected target

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polypeptide is held in its tertiary conformation by at least one disulfide bond.

14. The method of claim 1 wherein said target polypeptide is selected from the group consisting of growth factors, hormones, lymphokines, enzymes, antibody binding sites, viral proteins, non-enzymatically active procaryotic proteins, and analogs thereof.

15. A recombinant DNA encoding and capable of expressing a precursor fused polypeptide in a prokaryotic or eucaryotic organism, said DNA comprising:

a first DNA segment encoding a sequence of amino acids comprising a leader sequence, a hinge region, and at least one amino acid defining a cleavage site recognizable and cleavable by a selected cleavage agent,

said hinge region being cysteine-free and comprising at least two amino acids which promote cleavage by said cleavage agent at said cleavage site; and

a second DNA segment linked to said first segment encoding a sequence of amino acids defining a selected target polypeptide, whereby said cleavage site is a favored site for cleavage upon treatment of said fused polypeptide with said cleavage agent when said

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fused polypeptide is disposed in solution and said amino acid sequence defining a target polypeptide is disposed in its tertiary conformation.

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16. The recombinant DNA of claim 15 wherein said first DNA segment comprises DNA encoding a leader sequence comprising an amino acid sequence which imparts a preselected property to said fused polypeptide operable to facilitate concentration of said fused polypeptide.
 17. The recombinant DNA of claim 16 wherein said sequence of amino acids which imparts a selected property comprises an amphiphilic helix.
 18. The recombinant DNA of claim 15 wherein said cleavage site is immediately adjacent said target polypeptide.
 19. The recombinant DNA of claim 15 wherein said cleavage site comprises one or a sequence of amino acids absent from said sequence defining said target polypeptide.

20. The recombinant DNA of claim 15 wherein said cleavage site comprises a unique one or sequence of amino acids in said fused polypeptide.
21. The recombinant DNA of claim 15 wherein said cleavage site comprises a member selected from the group consisting of the cleavage site set forth in Table 1.
22. The recombinant DNA of claim 15 wherein said cleavage site comprises a Glu residue.
23. The recombinant DNA of claim 15 wherein said hinge region comprises at least one proline residue.
24. The recombinant DNA of claim 15 wherein said hinge region comprises an amino acid sequence which forms a random coil when said fused protein is disposed in aqueous solution.
25. The recombinant DNA of claim 15 wherein said hinge region includes a member selected from the group consisting of aspartic acid, glutamic acid, lysine, arginine, serine, proline, and combinations thereof, in amounts sufficient to render said hinge region soluble in water.

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26. The recombinant DNA of claim 15 wherein said second segment encodes a sequence of amino acids defining a target polypeptide, growth factors, hormones, lymphokines, enzymes, antibody binding sites, viral proteins, non-enzymatically active procaryotic proteins, and analogs thereof.

27. A fused polypeptide produced by an organism by expression of a recombinant DNA, said polypeptide comprising:

a first sequence of amino acids comprising a leader sequence, a hinge region, and at least one amino acid defining a cleavage site recognizable and cleavable by a selected cleavage agent, said hinge region being cysteine-free and comprising at least two amino acids which promote cleavage by said cleavage agent at said cleavage site, and a second sequence of amino acids linked to said first sequence and defining a selected target polypeptide, whereby said cleavage site is a favored site for cleavage upon treatment of said fused polypeptide with said cleavage agent when said fused polypeptide is disposed in solution and said second amino acid sequence is disposed in its tertiary conformation.

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28. The fused polypeptide of claim 27 wherein said leader sequence comprises a sequence of amino acids which imparts a preselected property to said fused polypeptide operable to facilitate concentration of said fused polypeptide.
29. The fused polypeptide of claim 28 wherein said sequence of amino acids which imparts a preselected property comprises an amphiphilic helix.
30. The fused polypeptide of claim 27 wherein said cleavage site is immediately adjacent said target polypeptide.
31. The fused polypeptide of claim 27 wherein said cleavage site comprises one or a sequence of amino acids absent from the sequence comprising said target polypeptide.
32. The fused polypeptide of claim 27 wherein said cleavage site comprises a unique one or sequence of amino acids in said fused polypeptide.
33. The fused polypeptide of claim 27 wherein said cleavage site comprises a member selected from the group consisting of the cleavage sites set forth in Table 1.

34. The fused polypeptide of claim 27 wherein said cleavage site comprises a Glu residue.
35. The fused polypeptide of claim 27 wherein said hinge region comprises at least one proline residue.
36. The fused polypeptide of claim 27 wherein said hinge region comprises an amino acid sequence which forms a random coil when said fused protein is disposed in aqueous solution.
37. The fused polypeptide of claim 27 wherein said hinge region includes a member selected from the group consisting of aspartic acid, glutamic acid, lysine, arginine, serine, proline, and combinations thereof in amounts sufficient to render said hinge region soluble in water.
38. The fused polypeptide of claim 27 wherein said second sequence of amino acids defines a target polypeptide selected from the group consisting of growth factors, hormones, lymphokines, enzymes, antibody binding sites, viral proteins, non-enzymatically active prokaryotic proteins, and analogs thereof.

39. A method of producing a biofunctional analog of a native form of a protein comprising at least one glutamic acid residue in a host cell culture, said method comprising the steps of:

- a. expressing a fused polypeptide by culturing said host cell culture, individual cells of said culture containing and being capable of expressing a recombinant DNA encoding said fused polypeptide, said fused polypeptide comprising
 - a first sequence of amino acids defining a leader sequence,
 - a second sequence of amino acids comprising said analog, said second sequence having an aspartic acid residue in place of at least one glutamic acid residue present in the native form of said protein, and
 - a glutamic acid residue linking said first and second sequence,
- b. exposing said fused polypeptide to S. aureus V-8 protease under conditions in which said protease favors cleavage at a glutamic acid residue over an aspartic acid residue to cleave said second sequence from said first sequence at the C-terminal side of said glutamic acid residue; and
- c. separating said first sequence from said second sequence.

40. The method of claim 39 comprising the additional step of exposing said fused polypeptide to renaturing conditions to dispose said second sequence in its folded conformation prior to step b.

41. The method of claim 40 wherein said first sequence is free of cysteine residues.

42. The method of claim 40 wherein said exposing step is conducted at alkaline pH in the presence of an ion selected from the group consisting of acetate and carbonate.

43. The method of claim 39 wherein said fused polypeptide further comprises a hinge region interposed between said first sequence and said second sequence adjacent said glutamic acid residue, said hinge region comprising at least two amino acids which promote access of said protease to said glutamic acid residue and including at least one amino acid selected from the group consisting of aspartic acid, arginine, lysine, proline, and serine, whereby the region of said fused polypeptide about said glutamic acid residue is soluble in water.

44. The method of claim 39 wherein said second sequence comprises a protein having an aspartic acid residue in place of a native glutamic acid residue present in the native form of said protein, said

protein being selected from the group consisting of growth factors, hormones, lymphokines, enzymes, antibody binding sites, viral proteins, non-enzymatically active prokaryotic proteins, and analogs thereof.

45. The analog produced by the method of claim 39.

46. The analog of claim 45 consisting of a calcitonin having an aspartic acid residue in place of a native glutamic acid residue.

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